

09/854,376

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(FILE 'HOME' ENTERED AT 15:24:05 ON 06 FEB 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 15:24:28 ON 06 FEB 2004

L1 14 S PTTG2  
L2 366091 S (INHIBIT? OR DIMINISH? OR DECREAS?) (6A) (NEOPLAS? OR CANCER? O  
L3 5 S L1 AND L2  
L4 5 DUP REM L3 (0 DUPLICATES REMOVED)

=> d bib ab 1-5 14

L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2003:777376 CAPLUS  
DN 139:287958  
TI Method of regulating biological activity of human pituitary tumor  
transforming gene (PTTG)1 using PTTG2  
IN Prezant, Toni Rita; Heaney, Anthony P.; Melmed, Shlomo  
PA USA  
SO U.S. Pat. Appl. Publ., 110 pp., Cont.-in-part of U.S. Ser. No. 777,422.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 12

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003186902	A1	20031002	US 2001-854326	20010511
	WO 9822587	A2	19980528	WO 1997-US21463	19971121
	W: JP, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6455305	B1	20020924	US 1999-894251	19990723
	US 2003018001	A1	20030123	US 2000-730469	20001204
	US 2002147162	A1	20021010	US 2001-777422	20010205
	WO 2001087935	A2	20011122	WO 2001-US15437	20010512
	WO 2001087935	A3	20020808		
	WO 2001087935	C2	20021227		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	WO 2001088116	A2	20011122	WO 2001-US15438	20010512
	WO 2001088116	A3	20020510		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1280906	A2	20030205		EP 2001-935430	20010512
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EP 1280907	A2	20030205		EP 2001-935431	20010512
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EP 1280908	A2	20030205		EP 2001-937309	20010512

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2003533988 T2 20031118 JP 2001-585324 20010512  
US 2003100530 A1 20030529 US 2002-264372 20021004

PRAI US 1996-31338P P 19961121  
WO 1997-US21463 W 19971121  
US 1999-894251 A2 19990723  
US 2000-569956 A2 20000512  
US 2000-687911 A2 20001013  
US 2000-730469 A2 20001204  
US 2001-777422 A2 20010205  
US 2001-854326 A 20010511  
WO 2001-US15255 W 20010512  
WO 2001-US15437 W 20010512  
WO 2001-US15438 W 20010512

AB Disclosed is a method of **inhibiting neoplastic**  
cellular **proliferation** and/or **transformation** of  
mammalian breast or ovarian cells, including cells of human origin, in  
vitro or in vivo. The inventive method involves the use of a pituitary  
tumor transforming gene (PTTG)2 peptide, which has the ability to regulate  
endogenous PTTG1 expression and/or function in a dominant neg. manner. In  
some embodiments, the invention is directed to gene-based treatments that  
deliver **PTTG2**-encoding polynucleotides to mammalian cells,  
whether in vitro or in vivo, to inhibit the endogenous expression of  
PTTG1. Other embodiments are directed to peptide-based treatments that  
deliver **PTTG2** peptide mols. to the cells, which inhibit  
endogenous PTTG1 expression and/or PTTG1 function. Kits useful in  
practicing the inventive method are also disclosed.

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:851361 CAPLUS

DN 136:622

TI Compositions and methods for modulating mammalian T-lymphocytes by  
targeted pituitary tumor transforming gene (PTTG) expression and/or  
function

IN Stoika, Rostyslav; Horwitz, Gregory A.; Zhang, Xun; Melmed, Shlomo

PA Cedars-Sinai Medical Center, USA

SO PCT Int. Appl., 185 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 12

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001088116	A2	20011122	WO 2001-US15438	20010512
	WO 2001088116	A3	20020510		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	US 2003018001	A1	20030123	US 2000-730469	20001204
	US 2002147162	A1	20021010	US 2001-777422	20010205
	US 2003186902	A1	20031002	US 2001-854326	20010511
	EP 1280907	A2	20030205	EP 2001-935431	20010512
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
	JP 2003533988	T2	20031118	JP 2001-585324	20010512
PRAI	US 2000-569956	A	20000512		
	US 2000-687911	A	20001013		

US 2000-730469	A	20001204
US 2001-777422	A	20010205
US 2001-854326	A	20010511
US 1996-31338P	P	19961121
WO 1997-US21463	W	19971121
US 1999-894251	A2	19990723
WO 2001-US15438	W	20010512

AB Disclosed is a method of **inhibiting neoplastic cellular proliferation** and/or **transformation** of mammalian T-lymphocyte cells, including cells of human origin, in vitro or in vivo. Also disclosed are methods of immunomodulating, i.e., inhibiting or inducing, the activation of T-lymphocytes by modulating gene PTTG (pituitary tumor transforming gene) expression and/or gene PTTG1 protein function. In vitro methods for screening substances for new immunosuppressing or immunoenhancing agents that modulate the activation of mammalian T-lymphocytes are disclosed. Also disclosed are useful compns. and kits. CDNA for human gene PTTG1 has been cloned based on sequence homol. with the rat PTTG gene. The rat and human genes and their encoded proteins have been investigated, including their mRNA expression in tissues and cell lines, transactivation of gene transcription, effects of overexpression on cell proliferation and tumor induction, regulation of human bFGF secretion, and identification of a human PTTG gene family. Gene PTTG1 and its encoded protein have transforming activity, in vitro and in vivo, which requires a proline-rich domain in the polypeptide C-terminal region. The transforming protein encoded by gene PTTG1 may function through SH3-mediated signal transduction. Human gene PTTG1 mRNA is overexpressed in most cancers, including tumors of the colon, breast, ovary, and myeloid lineages. Gene PTTG1 mRNA expression also increases upon T cell activation by anti-CD3 antibodies or phytohemagglutinin (PHA) in parallel with T cell proliferation, after IL-2 mRNA induction, and before cyclophilin mRNA induction. Immunosuppressants hydrocortisone and cyclosporin A inhibit PHA-stimulated gene PTTG1 expression and T cell proliferation in normal T cells, while cyclosporin A and TGF- $\beta$ 1 inhibit gene PTTG1 mRNA induction in activated leukemia cells. MRNA expression of gene PTTG1 is cell cycle-dependent in both T cells and a T cell leukemia line, with highest expression in G2/M-phase cells. Transfection of PHA-activated T cells with gene PTTG1 DNA encoding the C-terminal polypeptide region decreased the amount of S-phase cells and increased G2/M-phase cells.

L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:851203 CAPLUS

DN 136:691

TI Compositions and methods for modulating angiogenesis by regulated expression of pituitary tumor transforming gene (PTTG)

IN Heaney, Anthony P.; Ishikawa, Hiroki; Yu, Run; Horwitz, Gregory A.; Zhang, Xun; Melmed, Shlomo

PA Cedars-Sinai Medical Center, USA

SO PCT Int. Appl., 183 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 12

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001087935	A2	20011122	WO 2001-US15437	20010512
	WO 2001087935	A3	20020808		
	WO 2001087935	C2	20021227		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2003018001 A1 20030123 US 2000-730469 20001204  
US 2002147162 A1 20021010 US 2001-777422 20010205  
US 2003186902 A1 20031002 US 2001-854326 20010511  
EP 1280906 A2 20030205 EP 2001-935430 20010512

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI US 2000-569956 A 20000512  
US 2000-687911 A 20001013  
US 2000-730469 A 20001204  
US 2001-777422 A 20010205  
US 2001-854326 A 20010511  
US 1996-31338P P 19961121  
WO 1997-US21463 W 19971121  
US 1999-894251 A2 19990723  
WO 2001-US15437 W 20010512

AB Disclosed are compns. and methods of modulating angiogenesis in a tissue comprising mammalian cells, including cells of human origin, in vitro or in vivo. The compns. and methods also apply to enhancing wound healing and/or tissue regeneration and a method of limiting scar formation. CDNA for human gene PTTG1 (pituitary tumor transforming gene) has been cloned based on sequence homol. with the rat PTTG gene. The rat and human genes and their encoded proteins have been investigated, including their mRNA expression in tissues and cell lines, transactivation of gene transcription, effects of overexpression on cell proliferation and tumor induction, regulation of human bFGF secretion, and identification of a human PTTG gene family. Gene PTTG1 and its encoded protein have transforming activity, in vitro and in vivo, which requires a proline-rich domain in the polypeptide C-terminal region. The transforming protein encoded by gene PTTG1 may function through SH3-mediated signal transduction. Expression constructs with the C-terminal peptide of human gene PTTG1 block cell **transformation, inhibit tumor** formation in carcinoma cell lines and in nude mice, and suppress bFGF secretion. Human gene PTTG1 protein also exhibits angiogenic activity in assays using transfected cells.

L4 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:851202 CAPLUS

DN 136:4255

TI C-terminal peptides of the PTTG gene product and their use in **inhibition of neoplastic cellular proliferation or transformation**

IN Horwitz, Gregory A.; Zhang, Xun; HeaneyAnthony, P.; Melmed, Shlomo

PA Cedars-Sinai Medical Center, USA

SO PCT Int. Appl., 190 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 12

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001087934	A2	20011122	WO 2001-US15254	20010512
	WO 2001087934	A3	20020530		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

US 2003018001	A1	20030123	US 2000-730469	20001204
US 2002147162	A1	20021010	US 2001-777422	20010205
EP 1280905	A2	20030205	EP 2001-935340	20010512

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2003535612	T2	20031202	JP 2002-503274	20010512
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PRAI US 2000-569956 A 20000512  
US 2000-687911 A 20001013  
US 2000-730469 A 20001204  
US 2001-777422 A 20010205  
US 1996-31338P P 19961121  
WO 1997-US21463 W 19971121  
US 1999-894251 A2 19990723  
WO 2001-US15254 W 20010512

AB A method of **inhibiting neoplastic** cellular **proliferation** and **transformation** of mammalian cells using C-terminal peptides derived from the product of the PTTG (pituitary tumor transforming gene) gene is described. The peptides regulate the function of the protein and gene expression in a dominant neg. manner. The peptides may be used directly, as fusion proteins with uptake-promoting peptides, or expression vectors encoding the peptides may be used in gene therapy. The peptides may also increase the effectiveness of cytotoxic chemotherapeutic agents conventionally used to treat breast or ovarian cancers, thus allowing lower EDs of the agents to be administered. Kits comprising the inventive compns. are also disclosed for the treatment of neoplastic cellular proliferation in vitro or in vivo. Isolated PTTG-C peptides and PTTG-C-related polynucleotides are also disclosed, as are anti-PTTG-C-specific antibodies. Cloning and characterization of the PTTG gene and its role in neoplastic transformation is described. Two-hybrid assays showed that the PTTG gene product acted as a transcriptional activator. Deletion anal. identified the C-terminal region as important in regulating neoplastic transformation. This area is proline-rich and includes an SH3 domain.

L4 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2001:850858 CAPLUS  
DN 136:4254  
TI Pituitary tumor transforming gene 2 (PTTG2) and its role in the regulation of expression of pituitary tumor transforming gene 1  
IN Prezant, Toni Rita; Heaney, Anthony P.; Melmed, Shlomo  
PA Cedars-Sinai Medical Center, USA  
SO PCT Int. Appl., 175 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 12

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001087039	A2	20011122	WO 2001-US15255	20010512
	WO 2001087039	A3	20020321		
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	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	US 2003018001	A1	20030123	US 2000-730469	20001204
	US 2002147162	A1	20021010	US 2001-777422	20010205
	AU 2001063059	A5	20011126	AU 2001-63059	20010512
	EP 1280908	A2	20030205	EP 2001-937309	20010512

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI	US	2000-730469	A	20000120
	US	2000-569956	A	20000512
	US	2000-687911	A	20001013
	US	2001-777422	A	20010205
	US	1996-31338P	P	19961121
	WO	1997-US21463	W	19971121
	US	1999-894251	A2	19990723
	US	2001-854326	A	20010511
	WO	2001-US15255	W	20010512

AB Disclosed is a method of **inhibiting neoplastic** cellular **proliferation** and/or **transformation** of mammalian breast or ovarian cells, including cells of human origin, in vitro or in vivo. The inventive method involves the use of pituitary tumor transforming gene 2 (**PTTG2**) product, which has the ability to regulate endogenous PTTG1 expression in a dominant neg. manner. In some embodiments, the invention is directed to gene-based treatments that deliver **PTTG2**-encoding polynucleotides to mammalian cells, whether in vitro or in vivo, to inhibit the endogenous expression of PTTG1. Other embodiments are directed to peptide-based treatments that deliver **PTTG2** peptide mols. to the cells, which inhibit endogenous PTTG1 expression and/or PTTG1 function. Kits useful in practicing the inventive method are also disclosed.

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